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10/520,104	01/23/2006	Henry Daniell	10669-040	6977

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Timothy H. Van Dyke
390 No. Orange Avenue
Suite 2500
Orlando, FL 32801

EXAMINER	
KUBELIK, ANNE R	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/520,104	DANIELL, HENRY	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/24/09 & the revival of the application*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,10-25,33-49 and 51* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,10-25,33-49 and 51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 June 2009* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-6, 10-25, 33-49 and 51 are pending.

2. The objection to claims 6, 25, 35 and 51 because of informalities is withdrawn in light of Applicant's amendment of the claims.

3. The rejection of claims 9, 40 and 45-46 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement is withdrawn in light of Applicant's arguments.

4. The rejection of claims 1, 3-4, 7, 10, 12, 20, 23-27, 33 and 35-38 under 35 U.S.C. 102(b) as being anticipated by McBride et al (US Patent Publication 2002/0053094, filed July 1998) is withdrawn in light of Applicant's amendment of the claims.

5. The rejection of claims 1, 3-5, 7, 10-12, 15-17, 20, 23-27, 33, 35-38 and 47-49 under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Daniell (WO 99/10513 A1) is withdrawn in light of Applicant's amendment of the claims.

6. The rejection of claims 1, 3-4, 6-7, 10, 12-14, 18-20, 23-27, 33 and 35-38 under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of in view of Maliga et al (1999, US Patent 5,877,402) is withdrawn in light of Applicant's amendment of the claims.

7. The rejection of claims 1-4, 7, 10, 12, 20, 23-27, 33, 35-38 and 51 under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Chandrasegaran (1999, US Patent 5,792,640) is withdrawn in light of Applicant's amendment of the claims.

8. The rejection of claims 1, 3-4, 7-8, 10, 12, 20, 23-27, 33 and 35-39 under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Conkling et al (WO 98/56923) is withdrawn in light of Applicant's amendment of the claims.

9. The rejection of claims 9, 40 and 45-46 under 35 U.S.C. 103(a) as being unpatentable over McBride et al in view of Conkling et al as applied to claims 1, 3-4, 7-8, 10, 12, 20, 23-27, 33 and 35-39 above, and further in view of Aycock et al (1998, Crop Science 38:904) is withdrawn in light of Applicant's amendment of the claims.

10. The rejection of claims 21-22 under 35 U.S.C. 103(a) as being unpatentable over McBride et al in view of Daniell as applied to claims 1, 3-5, 7, 10-12, 15-17, 20, 23-27, 33, 35-38 and 47-49 above, and further in view of Rathinasabapathi et al (1994, Planta 193:155-162) is withdrawn in light of Applicant's amendment of the claims.

11. The rejection of claims 34 and 52 under 35 U.S.C. 103(a) as being unpatentable over McBride et al in view of Chandrasegaran as applied to claims 1-4, 7, 10, 12, 20, 23-27, 33, 35-38 and 51 above, and further in view of Reichert et al (1995, US Patent 5,460,956) is withdrawn in light of Applicant's amendment of the claims.

Claim Objections

12. Claim12 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the

claim(s) in independent form. Claim 12 fails to recite any structure that changes with the intended use of the vector; thus, claim 12 fails to further limit claim 1.

The objection is repeated for the reasons of record as set forth in the Office action mailed 24 October 2008. Applicant's arguments filed 24 June 2009 have been fully considered but they are not persuasive.

Applicant urges that the claim has been amended to delete "leucoplast" (response pg 7).

This is not found persuasive because Claim 12 fails to recite any structure that changes with the intended use of the vector in chloroplasts, vs chromoplasts, vs amyloplasts, vs proplastids vs etioplasts.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 1-6, 10-25, 33-49 and 51 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention. Dependent claims are included in all rejections. The rejection is different from the rejection set forth in the Office action mailed 24 October 2008, as applied to claims 4-5, 14, 16-17, 19, 25-27, 33-34, 45-49 and 51, and made because of Applicant's amendment to the claims. Applicant's arguments filed 24 June 2009 have been fully considered but they do not apply to this new rejection.

Claims 1, 35 and 51 are indefinite in their recitation of "IFNα2b" or a polypeptide having at least 95 percent sequence identity therewith". As no sequence identifier is given, there is no fixed sequence for the 95% identity comparison.

Claims 25 and 33 are indefinite in their recitation of "IFNα2b" or a polypeptide having at least 99 percent sequence identity therewith". As no sequence identifier is given, there is no fixed sequence for the 95% identity comparison. Further, as the vector of claim 1 encodes a protein of "IFNα2b" or a polypeptide having at least 95 percent sequence identity therewith", proteins with less than 99% identity would also be made by the method.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 1, 3-4, 12-13, 20, 23-25, 33, 35-39, and 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Reichert et al (1995, US Patent 5,460,956).

The claims are drawn to a plastid transformation and expression vector comprising an expression cassette comprising a plastid promoter, a selectable marker sequence, a heterologous DNA encoding IFNα2b, and a plastid transcription termination region, wherein the vector also comprises flanking sequences homologous to plastid DNA, and methods of using the vector in plastid transformation, and wherein the plant is Petit Havana.

McBride et al disclose plastid transformation vectors comprising regions of homology to a plastid genome flanking the selectable marker *aadA* and a construct comprising a plastid promoter operably linked to a sequence encoding interferon operably linked to a transcription termination region, plastids, plant cells, plants and seeds transformed with the construct and method of producing interferon in a plant cell (claims 1-2, 11, 25, 28-31). All plants are edible for some organism. The plastid transformation vectors also comprise 5' untranslated regions (claims 3-4).

McBride et al do not teach IFNα2b as the interferon.

Reichert et al teach IFNα2b (column 2, lines 49-65).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the plastid transformation and expression vectors encoding interferon taught by McBride et al to encode the interferon IFNα2b described in Reichert et al. One of ordinary skill in the art would have been motivated to do so because IFNα2b is a desirable form for disease treatment (Reichert et al, column 1, lines 15-32).

17. Claims 5, 10-11, 14-17, 19 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Reichert et al (1995, US Patent 5,460,956) as applied to claims 1, 3-4, 12-13, 20, 23-25, 33, 35-39, and 41-44 above, and further in view of Daniell (WO 99/10513 A1).

The claims are drawn to a plastid transformation and expression vector comprising an expression cassette comprising a plastid promoter, a selectable marker sequence, a heterologous DNA encoding IFNα2b, and a plastid transcription termination region, wherein the vector also

comprises flanking sequences homologous to plastid DNA, and methods of using the vector in plastid transformation, and wherein the plant is Petit Havana.

The teachings of McBride et al in view of Reichert et al are discussed above. McBride et al in view of Reichert et al do not teach flanking sequences homologous to transcriptionally active spacer regions in the plastid DNA, including *trnI* and *trnA*.

Daniell teaches a plastid transformation and expression vector comprising an expression cassette comprising the *Prrn* (16SrRNA) plastid promoter, a selectable marker sequence (*aadA*), a heterologous DNA encoding a pharmaceutical protein, and a plastid transcription termination region (*psbA* 3'), wherein the vector also comprises flanking sequences homologous to transcriptionally active spacer regions in the plastid DNA and to a single copy a region (the *rbc1* and *orf512* genes or the *trnI* and *trnA* genes), methods of using the vector in plastid transformation, and Petit Havana tobacco plants, seed and progeny thereby obtained (pg 26, lines 29-37; pg 29, line 19, to pg 33, line 19; pg 42, line 10, to pg 43, line 26; pg 51, line 12, to pg 60, line 9; Fig 3A; claims 1-2, 85-86, 100-103 and 111-113). The transcription termination region is a 3' untranslated region capable of conferring transcript stability to the protein. The plastids in tobacco leaves would be chloroplasts. Tobacco is edible.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the plastid transformation and expression vectors taught by Daniell, to encode IFNα2b as described in McBride et al in view of Reichert et al. One of ordinary skill in the art would have been motivated to express IFNα2b in Daniell vectors over those taught by McBride because of the superiority of the Daniell vectors (pg 6, line 28, to pg 7, line 7; pg 9, line 1, to pg 10, line 3, pg 11, lines 9-18) and because of the suggestion of Daniell to express

high-value biopharmaceutical proteins in plastids using his vectors (pg 13, line 26, to pg 14, line 22; pg 30, line 30, to 33, line 19). It would be obvious to one of skill in the art to express a human interferon like IFNα2b, as this is the most economically desirable form. At least some plants would produce IFNα2b at about 18.5% total soluble protein, and it would be obvious to one of skill in the to select for plants that produced IFNα2b at that rate or higher, to increase the yield of this economically desirable product.

18. Claims 5-6 and 14-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Reichert et al (1995, US Patent 5,460,956) as applied to claims 1, 3-4, 12-13, 20, 23-25, 33, 35-39, and 41-44 above, and further in view of Maliga et al (1999, US Patent 5,877,402).

The claims are drawn to a plastid transformation and expression vector comprising an expression cassette comprising a plastid promoter, the *psbA* 5' and/or 3' untranslated region or the *psbA* or Prrn (16S rRNA) promoter, a selectable marker sequence, a heterologous DNA encoding IFNα2b, and a plastid transcription termination region, wherein the vector also comprises flanking sequences homologous to plastid DNA, and methods of using the vector in plastid transformation.

The teachings of McBride et al in view of Reichert et al are discussed above. McBride et al in view of Reichert et al do not teach *psbA* 5' and 3' UTRs in the vector.

Maliga et al teach plastid transformation and expression vectors comprising *psbA* 5' and 3' untranslated regions and the *psbA* and Prrn promoters (Fig 22B and C).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the plastid transformation vector taught by McBride et al in view of Reichert

et al, to include the *psbA* 5' and 3' untranslated region described in Maliga et al. One of ordinary skill in the art would have been motivated to do so because of the ribosome binding sites present (Maliga et al, column 24, lines 63, to column 25, line 3) and because use of the *psbA* 5' UTR resulted in high expression levels (column 62, lines 56-65). Selection of the *psbA* 3' UTR is a design choice from among commonly used 3' UTRs in plastid transformation vectors. Selection of the*psbA* or Prrn promoter is a design choice from among commonly used promoters in plastid transformation vectors.

19. Claims 2, 34 and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Reichert et al (1995, US Patent 5,460,956) as applied to claims 1, 3-4, 12-13, 20, 23-25, 33, 35-39, and 41-44 above, and further in view of Chandrasegaran (1999, US Patent 5,792,640).

The claims are drawn to a plastid transformation and expression vector comprising an expression cassette comprising a plastid promoter, a selectable marker sequence, a heterologous DNA encoding IFNα2b comprising a histidine tag and a thrombin cleavage site, and a plastid transcription termination region, wherein the vector also comprises flanking sequences homologous to plastid DNA, and methods of using the vector in IFNα2b production from plant cells.

The teachings of McBride et al in view of Reichert et al are discussed above. McBride et al in view of Reichert et al do not teach a histidine tag and a thrombin cleavage site in the interferon.

Chandrasegaran teaches expression of heterologous protein in plant cells, wherein the heterologous protein has a histidine tag and a thrombin cleavage site (column 9, lines 50-59).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of expressing IFNα2b in plant cell plastids as taught by McBride et al, to include a histidine tag and a thrombin cleavage site as described in Chandrasegaran. One of skill in the art would also use IFNα2b comprising a polyhistidine tag and thrombin cleavage site because of the ease of isolation the histidine tag affords and the desire to remove the tag after isolation.

20. Claims 40 and 44-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Reichert et al (1995, US Patent 5,460,956) as applied to claims 1, 3-4, 12-13, 20, 23-25, 33, 35-39, and 41-44 above, further in view of Conkling et al (WO 98/56923) and further in view of Aycock et al (1998, Crop Science 38:904).

The claims are drawn to a plastid transformation and expression vector comprising an expression cassette comprising a plastid promoter, a selectable marker sequence, a heterologous DNA encoding IFNα2b, and a plastid transcription termination region, wherein the vector also comprises flanking sequences homologous to plastid DNA, and methods of using the vector in plastid transformation, wherein the plant is low-nicotine tobacco.

The teachings of McBride et al in view of Reichert et al are discussed above. McBride et al in view of Reichert et al do not teach using a low nicotine tobacco for production of pharmaceutical proteins or low nicotine tobacco LAMD-609.

Conkling et al teach that a low nicotine tobacco are very attractive for production of pharmaceutical proteins (pg 1, line 12-16; pg 6, line 26, to pg 7, line 2).

Aycock et al teach the low nicotine tobacco LAMD-609.

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the method of expressing interferon in plant cell plastids taught by McBride et al to use low nicotine tobacco plants as described in Conkling et al. One of ordinary skill in the art would have been motivated to do so because tobacco that does not produce nicotine would have more resources available fir production of the transgene product (Conkling et al pg 6, line 26, to pg 7, line 2) and the nicotine would not be a contaminant in the product. Low-nicotine tobacco would be edible for mammalian consumption.

It would have been obvious to one of ordinary skill in the art to use LAMD-609 taught by Aycock et al as the low nicotine tobacco. One of ordinary skill in the art would have been motivated to do so because selection of one low nicotine tobacco over another is an obvious design choice.

21. Claims 21-22 rejected under 35 U.S.C. 103(a) as being unpatentable over McBride et al (US Patent Publication 2002/0053094, filed July 1998) in view of Reichert et al (1995, US Patent 5,460,956) as applied to claims 1, 3-4, 12-13, 20, 23-25, 33, 35-39, and 41-44 above, and further in view of Rathinasabapathi et al (1994, Planta 193:155-162).

The claims are drawn to a plastid transformation and expression vector comprising an expression cassette comprising a plastid promoter, a selectable marker sequence, a heterologous DNA encoding IFNα2b, and a plastid transcription termination region, wherein the vector also comprises flanking sequences homologous to plastid DNA, and wherein the selectable marker is BADH.

The teachings of McBride et al in view of Reichert et al are discussed above. McBride et al in view of Reichert et al do not teach use of BADH as a selectable marker.

Rathinasabapathi et al teach transformation of tobacco plants with a spinach or beet gene encoding BADH (pg 157). The protein is targeted to the chloroplasts (pg 157-158) and the resulting plants are resistant to betaine aldehyde (pg 159-160).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify the vectors taught by McBride et al in view of Daniel to use the BADH gene as a selectable marker as described in Rathinasabapathi et al. One of ordinary skill in the art would have been motivated to do so because of the suggestion of Rathinasabapathi et al to use betaine aldehyde resistance as a selectable marker in plants that lack glycine betaine (paragraph spanning the columns, pg 161) and because substitution of chloroplast transformation for chloroplast targeting of a nuclear-encoded gene is an obvious design choice.

Conclusion

22. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, Ph.D., whose telephone number is (571) 272-0801. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached at (571) 272-0975.

The central fax number for official correspondence is (571) 273-8300.

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USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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August 7, 2009

/Anne R Kubelik/
Primary Examiner, Art Unit 1638